Available online at www.sciencedirect.com
SCIENCE DIRECT®
Analytica Chimica Acta 507 (2004) 3–10
ANALYTICA CHIMICA ACTA
www.elsevier.com/locate/aca

Microchip devices for detecting terrorist weapons

Joseph Wang*

Department of Chemistry and Biochemistry, New Mexico State University, Box 30001-Dept. 3C, Las Cruces, NM 88003, USA

Received 6 August 2003; accepted 11 August 2003

Abstract

Escalating threats of terrorist activity have led to urgent demands for innovative devices for on-site detection of chemical and biological agents and explosive materials. Field detection of such hazardous substances requires that a powerful analytical performance be coupled to miniaturized low-powered instrumentation. "Lab-on-a-Chip" devices, where liquids are manipulated in a microchannel network, offer great promise for converting large and sophisticated instruments into powerful field-deployable analyzers. Particularly attractive for on-site security applications is the very small footprint of microchip devices, high degree of integration, high performance, fast response, and versatility. This article reviews a variety of microchip-based protocols and devices for detecting terrorist weapons. Such microfluidic devices offer great promise for transporting the forensic laboratory to the sample source, and providing an early warning prior to terrorist activity, or a rapid post-analysis 'fingerprints' of a disaster site. Due to the small footprint of microchip devices, it could be possible to perform multiple assays simultaneously. Such prospects, challenges and applications are discussed.

Keywords: Microchip devices; Explosives; Nerve agents; Biothreat agents

1. Introduction

Growing concerns regarding terrorist activity have generated tremendous demands for innovative field-portable tools capable of detecting warfare agents and explosive compounds, in a faster, simpler, and reliable manner at the site of terrorism [1]. On-site real-time monitoring is urgently needed to protect the health and safety of society, for ensuring our food safety, and protect the water supply systems. For example, a rapid and sensitive detection of chemical and biological warfare agents could provide an early alarm of their release, hence minimizing further spread and civilian casualties. Point-of-care diagnosis of individuals potentially exposed to such threat agents, will allow first-responder health providers to react quickly and efficiently to provide optimal and case-appropriate health care, and convince unexposed individuals of their health safety. Highly sensitive field measurements of low- and high-energy explosives are urgently needed to support various surveillance activities and investigation of bombing sites. 'Counter-terrorism' detection systems should thus offer high sensitivity and selectivity, a fast response, low false alarms, portability and low-power requirements. Today's systems are too bulky or slow to meet the "detect to warn" needs for civilians or soldiers. Designing miniaturized field-deployable devices that retain the high sensitivity and selectivity of sophisticated laboratory-based instruments represents a major analytical challenge.

The aim of the present article is to review recent efforts towards the development of microchip devices for detecting explosive compounds and chemical and biological warfare agents. Microfabricated microfluidic analytical devices, integrating multiple sample handling processes with the actual measurement step, represent the fastest developing field in analytical chemistry and hence are of considerable recent interest [2,3]. Such devices, referred to as "Lab-on-a-Chip" devices, offer tremendous potential for obtaining the desired forensic information in a faster, simpler, and cheaper manner compared to traditional laboratory-based instruments. "Lab-on-a-Chip" devices are fabricated using planar glass and polymer substrates, with a cover plate used for closing the microchannel network in the etched plate. The microfabrication process facilitates the integration of a short separation channel with functional elements, such as mixing tees and cross intersections for mixing reagents and injecting samples with high speed and reproducibility. Such fluid flow and reagent mixing are accomplished via electrokinetic

* Tel.: +1-505-6462140; fax: +1-505-6466033.
E-mail address: joewang@nmsu.edu (J. Wang).

0003-2670/$ – see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/j.aca.2003.08.031

transport (which is the combined effect of electroosmosis and electrophoresis), without the use of external pumps and valves. This is accomplished by regulating the applied voltages at the terminus of each channel of the microchip. Capillary electrophoresis (CE) has proven to be particularly suited for high-speed microchip separations. Compounds are separated based on their mass-to-charge ratios; neutral ones require an addition of a charged surfactant to the run buffer.

"Lab-on-a-Chip" technology holds great promise for converting large and sophisticated laboratory-based instruments into powerful field-portable analyzers. Particularly attractive for on-site homeland-defense applications is the very small footprint of microfluidic devices, their very fast response, high degree of integration, versatility, and high performance. Complete assays, involving sample pretreatment (e.g. preconcentration/extraction), chemical/biochemical derivatization reactions, electrophoretic separations, and detection, have been realized on single microchip platforms [2,3]. Highly effective separations combined with short assay times have been achieved by combining long separation channels and high electric fields. The small footprint of microchip devices permits the adaptation of highly parallel assays (in multi-channel manifolds), which opens the door to simultaneous monitoring of various classes of terrorist weapons. The versatility of such on-chip assays offers great promise for conducting novel operations relative to homeland security, e.g. rapid switching between rapid screening and fingerprint identification [4]. Advances in the areas of microfluidics and microfabrication over the past decade have led to microchip analytical devices with a broad range of functionality and versatility [2,3]. Newly developed microfluidic devices offer great promise for providing an early and rapid warning and alarm prior to terrorist activity, as well as a fast post-analysis 'fingerprints' of a disaster site.

The successful deployment of 'counter-terrorism' microchip analytical devices requires proper attention to the issues of continuous sampling (through effective 'world-to-chip' interfaces) and on-chip sample pretreatment (cleanup, preconcentration, etc.). In the following sections we will discuss the prospects, opportunities and challenges of developing chip-based detection devices for explosive substances and chemical or biological warfare agents.

2. Microchip devices for monitoring explosives

There are urgent security needs for a rapid and sensitive detection of explosives for supporting various 'counter-terrorism' surveillance activities. Such activities include the detection of hidden explosives and investigation of bombing scenes [5]. Post-explosion analysis is of great importance for such investigations, particularly for connecting between cases and suspects. Various chip-based protocols have shown useful for fast and sensitive measurements of low-energy ionic explosives and high-energy organic explosives. The latter require separation by micellar electrokinetic chromatography in connection to electrochemical or fluorescence detection.

Efforts aimed at the microchip-explosive detection were initiated at the Sandia National Laboratory [6]. These efforts have led to a portable self-contained system (MicroChemLab^{TM}) capable of monitoring nitroaromatic explosives in both gas and liquid phases in connection to a variety of separation and detection schemes. The Sandia's microsystem also integrates sampling (from the real world) and has been expanded to the detection of biotoxins. Wallenberg and Bailey [7] combined a MEKC separation on a glass chip with indirect laser-induced-fluorescence detection for rapid measurements of nitroaromatic compounds in environmental samples. A 65 mm long separation channel offered complete separation of 10 explosives within 1 min (in connection to 60,000 theoretical plates) in connection to the Cy7-dye visualizing agent. For example, Fig. 1 displays the separation and detection of 14 explosives in an EPA 8330 mixture using a separation voltage of 4000 V. An epi-fluorescence detection setup was employed, with excitation provided by a near IR diode laser operating at 750 nm.

Self-contained CE microchips, based on electrochemical detection, are extremely attractive for on-site security applications owing to the inherent miniaturization, high performance, low cost and minimal power demands of such detectors. The inherent redox activity of nitroaromatic explosives make them ideal candidates for electrochemical monitoring. Such organic explosives are readily reduced at low potentials at various working electrode materials. Our group and that of Luong have developed several effective CE/amperometric microchip protocols for detecting nitroaromatic explosives down to the ppb level [4,8–10]. Such amperometric detection relies on the application of a fixed (negative) potential at the working electrode (to drive the electron-transfer reaction), and monitoring the reduction current as a function of time. The current response thus generated reflects the concentration profiles of these explosives as they pass over the detector. A surfactant, such as sodium dodecyl sulfate (SDS) is commonly added to the run buffer to facilitate the separation of the neutral nitroaromatic explosives. Hilmi and Luong [9] employed a gold working electrode, formed by electroless deposition onto the chip capillary outlet, for highly sensitive amperometric detection of nitroaromatic explosives (with a detection limit of 24 ppb TNT). Analysis of a mixture of four explosives (TNT, 2,4-DNT, 2,6-DNT and 2,3-DNT) was accomplished in around 2 min, using a detection potential of −0.8 V and a borate/SDS buffer. Wang et al. [10] described the use of diamond working electrodes for imparting high sensitivity and stability onto amperometric detection of nitroaromatic compounds following their CE microchip separations. The enhanced stability was indicated from a RSD of 0.8% for 60 repetitive measurements of 5 ppm 2,4,6-trinitrotoluene.

Further lowering of the detection limits of these optical and electrochemical explosive detection schemes can be accomplished by integrating on-chip preconcentration

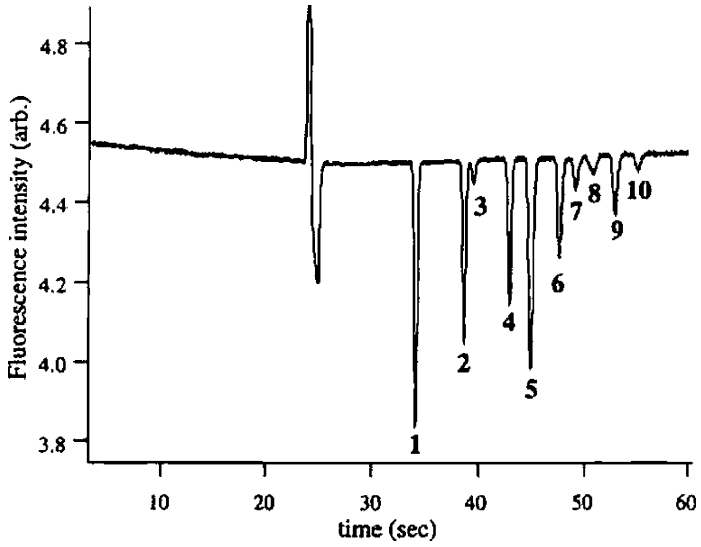

Fig. 1. Separation and detection of a mixture of nitroaromatic and nitramine explosives on a microchip with micellar electrokinetic chromatography and indirect laser-induced fluorescence. Analytes: 20 ppm TNB (1), DNB (2), NB (3), TNT (4), tetryl (5), 2,4-DNT (6), 2,6-DNT (7), 2-, 3- and 4-NT (8), 2-Am-4,6-DNT (9), and 4-Am-2,6 DNT (10) (from Ref. [7] with permission).

elements. In particular, Collins and coworkers [11] described a microscale, semi-automated solid-phase extraction (SPE) system for explosives. The SPE microcolumn was constructed from a Teflon tubing packed with the SPE material. The collected explosives were eluted into 5 μl acetonitrile to provide ng/l detection limits.

Convenient distinction between 'total' and 'individual' explosive compounds has been accomplished in connection to chip-based 'flow-injection' (fast-screening) and the 'separation' (fingerprint-identification) operation modes [4]. The realization of such dual-mode (flow-injection/separation) protocol using a single microchannel chip manifold involved a rapid switching from a run buffer that did not contain sodium dodecyl sulfate (SDS) to an SDS-containing buffer. As desired for various forensic and defense scenarios, this allowed repetitive high-speed screening assays of the 'total' content of explosive compounds, and switching to the detailed fingerprint identification once such substances were detected. Fig. 2 illustrates such 'total' and 'individual' measurements for a mixture of nitroaromatic organic explosives. Applicability to nerve-agent compounds was also demonstrated.

In addition to high-energy organic explosives, chip-based devices offer great promise for separating and detecting explosive-related ions [12]. A new contactless-conductivity detection system has been particularly useful for this task. Such detector can sense all ionic species having conductivity different from the background electrolyte. The low electroosmotic flow (EOF) of the poly(methylmethacrylate) (PMMA) chip material facilitated the rapid switching between analyses of explosive-related cations and anions using the same microchannel and run buffer (and without an EOF modifier); this led to a rapid (<1 min) measurements of seven explosive-related cations and anions down to the low micromolar level. Addition of a 18-crown-6 ether modifier has been used for separating the peaks of co-migrating potassium and ammonium ions. In addition to sequential injection of anionic and cationic explosives, it is possible to use a special chip-based dual-end opposite injection protocol for simultaneous measurements of explosive-related cations and anions [13]. For this purpose, mixtures of anions and cations were injected simultaneously from both sides of the chip to the separation channel, so that the cations and anions migrated in opposite directions and detected in the center of the separation channel by a movable contactless-conductivity detector. Simultaneous measurements of explosive-related ions and nerve-agent degradation products were also documented.

A new dual electrochemical microchip detection system, based on the coupling of conductivity and amperometric detection methods facilitated the simultaneous measurements

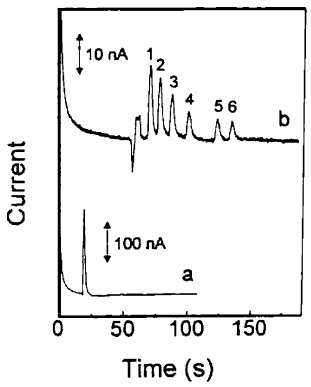

Fig. 2. Electropherograms depicting the 'total' (a) and 'individual' (b) assays for mixtures of nitroaromatic explosives. Analytes: TNB (1), DNB (2), TNT (3), 2,4-DNT (4), 2-Am-4,6-DNT (5), and 4-Am-2,6-DNT (6); 10 ppm each (from Ref. [4] with permission).

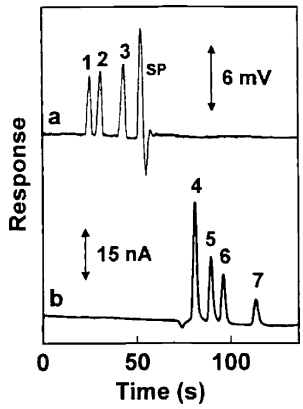

Fig. 3. Simultaneous CE microchip measurements of low- and high-energy explosives as recorded with a dual conductivity (a) and amperometric (b) detectors. Analytes: methyl-ammonium (1), methylammonium (2), sodium (3), TNB (4), TNT (5), 2,4-DNB (6), and 2-Am-4,6-DNB (7); system peak (SP) (from Ref. [14] with permission).

of both nitroaromatic and ionic explosives [14]. The microsystem relied on the combination of a contactless conductivity detector with an end-column thick-film carbon amperometric detector. Its ability to monitor both redox-active nitroaromatic and ionic explosives is illustrated in Fig. 3. The total assay of this seven explosive-related mixture is performed within less than 2 min.

Bromberg and Mathies [15] have recently coupled homogeneous immunoassays with microfabricated CE devices for highly sensitive detection of TNT and its derivatives. The electrophoretic competitive immunoassay was based on the rapid separation of an equilibrated mixture of an anti-TNT antibody, fluorescein-labeled TNT, and unlabeled TNT. Such chip-based immunoassay offered a wide dynamic range (1–300 ng/ml), with a detection limit of 1 ng/ml. Kinetic assays were employed for determining the binding and dissociation constants. As will be described below, on-chip immunoassays offer also great promise for on-site detection of biothreat agents.

3. Microchip devices for detecting CWA

In response to recent terrorist activity, there are urgent demands for highly sensitive, rapid and reliable methods for on-site measurements of chemical warfare agents (CWA) and their degradation products [16].

Nerve agents derive their name from their adverse effect on the nervous system. Several papers have demonstrated the utility of microchip devices for detecting CWA. Ramsey and coworkers described microfluidic assays of acetylcholinesterase (AChE) inhibitors, integrating the sequential steps of such inhibition protocols onto the microchip platform [17]. AChE inhibitors were monitored from the decreased fluorescence signal of the thiocholine product. Such negative peaks are diagnostic of competitive and irreversible inhibition processes. Four cationic inhibitors of AChE were thus separated electrophoretically and detected within 70 s

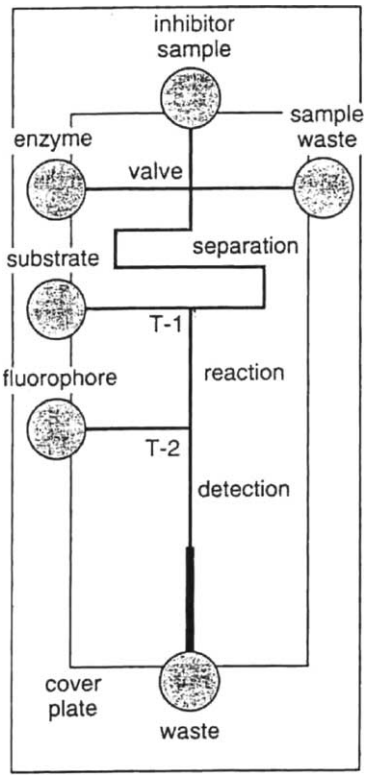

Fig. 4. Schematic of the enzyme-based chip for measuring inhibitors. The channels terminate at reservoirs containing the indicated solutions (from Ref. [17] with permission).

(Fig. 4). In addition, a stopped-flow protocol was employed for extending the reaction time of irreversible inhibitors (to 5 min) and lowering the detection limits (e.g. down to 10 nM carbofuran). A CE-microchip, based on an amperometric detection, has been employed for monitoring organophosphorous (OP) compounds [18]. Such non-enzymatic device relied on the CE separation of organophosphorous pesticides followed by their reductive detection at an end-column thick-film carbon-electrode detector. Such microchip detection of OP compounds has been combined with rapid switching between rapid (flow-injection) screening and fingerprint (separation) identification [4].

A chip-based CE/conductivity microfluidic device was recently developed for fast screening of CWA degradation products [19]. The miniaturized system relies on an efficient chip-based separations of alkyl methylphosphonic acids (breakdown products of Sarin, Soman, and VX nerve-agents) followed by their sensitive contactless conductivity detection. The new microsystem couples high sensitivity, with a fast response, good precision and a wide linear range. For example, Fig. 5B displays an electropherogram for a river sample, spiked with 20 ppm methylphosphonic acid (a), ethyl methylphosphonic acid (b), and isopropyl methylphosphonic acid (c). Three well-defined and baseline-resolved peaks are observed for these nerve-agent degradation products. The total assay time is around 130 s. Note, the flat baseline and the absence of background interferences (Fig. 5A).

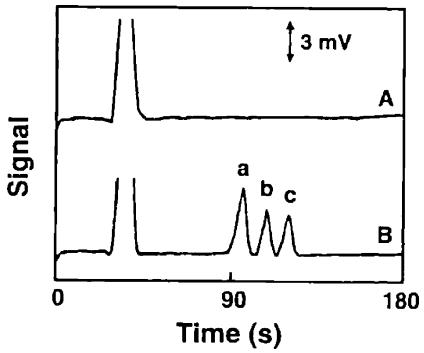

Fig. 5. Microchip conductivity detection of CWA degradation products. Electropherogram for a river water sample before (A) and after (B) the addition of 20 ppm MPA (a), EMPA (b) and IMPA (c). The untreated sample was filtered and spiked with the required amounts of MES/His buffer (to yield a 5 mM level and pH of 6.1) (from Ref. [19] with permission).

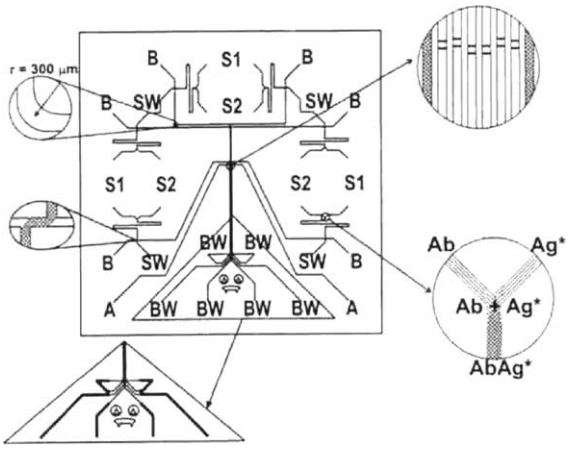

Fig. 6. Layout of the flow manifold for a six-channel microfluidic immunoassay device. Each reaction cell has reservoirs for the sample (S1), antibody (S2), and the sample injection waste (SW) (from Ref. [22] with permission).

Qiu and Collins reported recently on the microchip fluorescence detection of cyanide [20]. Such detection was accomplished by using the reaction of cyanide with 2,3-naphthaldehyde and taurine to form a fluorescent derivative. The latter was separated on a CE microchip and detected utilizing a violet diode laser excitation source, thereby maintaining the potential portability of this detection microsystem.

4. Detection of biothreat agents

Biological agents such as bacteria, viruses or toxins, have long been used as tools of terrorism. Hence, there are urgent needs for portable field-deployable highly sensitive fast-responding detection devices capable of rapidly identifying and quantifying broad classes of biological warfare agents (BWA). Such fast and sensitive pathogen detection could provide an early warning of their release, hence minimizing further spread and human casualties. Early detection of bioagents is also essential for protecting our water resources and food supplies in defense against terrorist activity.

The coupling of 'Lab-on-a-Chip' technology with novel detection biochemistry offers great promise for BW threat detection and diagnosis. Microchip devices could provide early/rapid/timely, reliable and simultaneous on-site identification and quantitation of biothreat agents. For example, the Sandia's MicroChemLab has been expanded for biotoxin detection down to the nanomolar level [16]. Such biotoxin two-channel device utilizes microchip CE and gel electrophoresis to provide orthogonal analysis in connection to a LIF detection. Two chip-based routes, involving immunoassays and genetic testing, are being evaluated for this task.

4.1. On-chip immunoassays

Recent activity has led to the development of immunoassays for detecting BWA [21]. Immunoassays rely on the shape recognition of the analyte (antigen) by the antibody binding site to form the antibody–antigen complex. Such assays allow measurements of trace amounts of analytes in complex samples. Conventional immunoassays are slow and involve various liquid-handling steps. Chip-based immunoassays, combine the selectivity and sensitivity features of antibody–antigen interactions with the analytical power, integration, versatility and reagent economy of microfluidic devices, and hence should have a major impact upon the detection of BW agents. Harrison and coworkers [22] reported an integrated six-channel microfabricated device for performing reagent/sample mixing, immunological reaction, and affinity capillary electrophoresis (ACE) separation (Fig. 6). The resulting assays were conducted within less than 60 s and offered nanomolar detection limits. The same group developed a stand-alone, automated microfluidic-based instrument platform for immunoassays [23]. The complete system performed key steps, including sampling, injection, mixing, separation, detection and elimination within ca. 3–5 min. A robust performance with run-to-run migration time reproducibility of 0.21% (3% over 14 days), excellent chip durability, and fluorescence detection limits of 0.21 nM were observed. Compact subsystems for the optical detection, high voltage, fluidic interface, and computer control were designed, so that the entire system could fit into a portable 30 cm × 35 cm × 50 cm box.

Recent work from our laboratory [24] demonstrated an electrochemical enzyme immunoassay protocol based on the on-chip integration of a pre-column immunological reaction, electrophoretic separation, with a post-column enzymatic reaction (Fig. 7). The separation of the enzyme-labeled antibody from the enzyme-labeled antibody–antigen pair was followed by post-column addition of the appropriate substrate. Amperometric detection of the liberated aminophenol product yielded a remarkably low detection limit of 1.7×10^{-18} M for the mouse IgG model analyte. A bead-based enzyme electrochemical immunoassay microsystem for

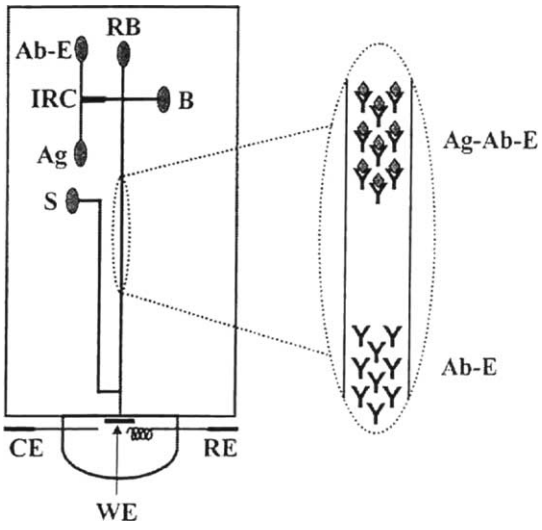

Fig. 7. Schematic of the microchip for electrochemical enzyme immunoassays: RB, running buffer; B, unused buffer reservoir; Ab-E, enzyme-labeled antibody; Ag, antigen; S, substrate; IRC, immunoreaction chamber; RE, reference electrode; CE, counter electrode; WE, working electrode (from Ref. [24] with permission).

detecting pathogenic organisms is being developed by Heineman and coworkers [25]. Such system uses flow-through reaction chambers in which beads are held magnetically while the necessary reagents and rinsing solutions are flowing through. It relies on the use of sandwich-enzyme (alkaline phosphatase) immunoassay along with amperometric detection of the *p*-aminophenol product. The total system has five reservoirs for reagents, two reaction chambers, and a detection chamber, all of which are connected by silicone tubing. Bead-based microchip immunoassays were also developed by Kitamori and coworkers [26]. Such protocols relied on placing polystyrene beads, coated with the antibody, into the microchannel, along with heterogeneous immunoassay, and optical detection of the colloidal gold tracer.

4.2. DNA-microchip analysis

Nucleic acid recognition offers unique possibilities for the identification of pathogenic organisms. The application of microfabricated devices to the field of DNA diagnostics holds great promise for on-site BWA detection. Several studies have demonstrated the ability to integrate multiple steps, including DNA extraction, PCR amplification, with nucleic acid separation or hybridization and detection on a single microchip platform [27–30].

On-chip integration of PCR amplification represents a challenge owing to the need for large temperature changes, related bubble formation, and compatibility of the enzyme involved with the chip material. Mathies and coworkers reported a microfabricated DNA analysis device, integrating PCR amplification and CE analysis [27]. Such coupling offered a rapid thermal cycling capability of a silicon PCR reactor (10 °C/s heating, 2.5 °C/s cooling) along with high speed (<2 min) DNA separations at the glass CE chip. Tang et al. [28] described an integrated four-channel microfluidic electrophoretic system for analyzing genetic materials in connection to an isothermal cyclic probe amplification technology and a LIF detection. Such integrated cyclic probe device offered an amplification factor of 42,000 and hence led to fM detection limits. Disposable plastic (polycarbonate) devices, integrating PCR amplification and DNA hybridization, were developed by Motorola Inc. [29]. Such integrated devices rely on the use of Pluronics phase change valves to meet the requirements of on-chip microvalves. Landers and coworkers [30] reported an efficient microchip-based solid-phase extraction (SPE) method for purifying DNA from biological samples. Fig. 8 demonstrates the ability of such microchip SPE procedure, in connection to on-chip fluorescence detection, for providing rapid purification of bacterial DNA from the vaccine strain of *B. anthracis* (anthrax). Belgrader et al. [31] developed a minisonicator to for rapid lysis of anthrax spores in connection microchip PCR amplification. The total assay time (including the spore disruption) was 15 min.

5. Sampling and sample pretreatment

Crucial for the successful realization of such effective ‘counter-terrorism’ detection devices is the development of effective “world-to-chip” interfaces. Such interfaces are essential for obtaining a timely analytical data, essential for triggering an alarm for making a proper protective action. Sampling of both air and water samples is thus essential for portable defense diagnostic devices.

A recent contribution from Harrison and coworkers [32] demonstrated a convenient interface of microfluidic devices to the external environment. Such interface design facilitates the sample introduction into an electrokinetic microchip (without perturbing the liquids within the microfluidic device), through the use of an interface flow channel with a significantly lower volume flow resistance. Fang and coworkers [33] developed a high-throughput continuous sample introduction interface for microchip devices based on a flow-through sampling reservoir featuring a guided overflow design. High stability was reported over a prolonged 4 h period, involving 166 analytical cycles. Such ability to continuously introduce real samples into micrometer channels would make “Lab-on-a-chip” devices compatible with real-life security and forensic applications.

The integration of sample pretreatment into microfabricated devices is also crucial for the deployment of field-portable monitors for terrorist weapons. The versatile nature of microfluidic devices provides opportunities to conduct different sample pre-treatment procedures relevant for such detection, including preconcentration or cleanup [34,35]. Sample preconcentration is often required to achieve lower detection limits or to minimize potential interferences.

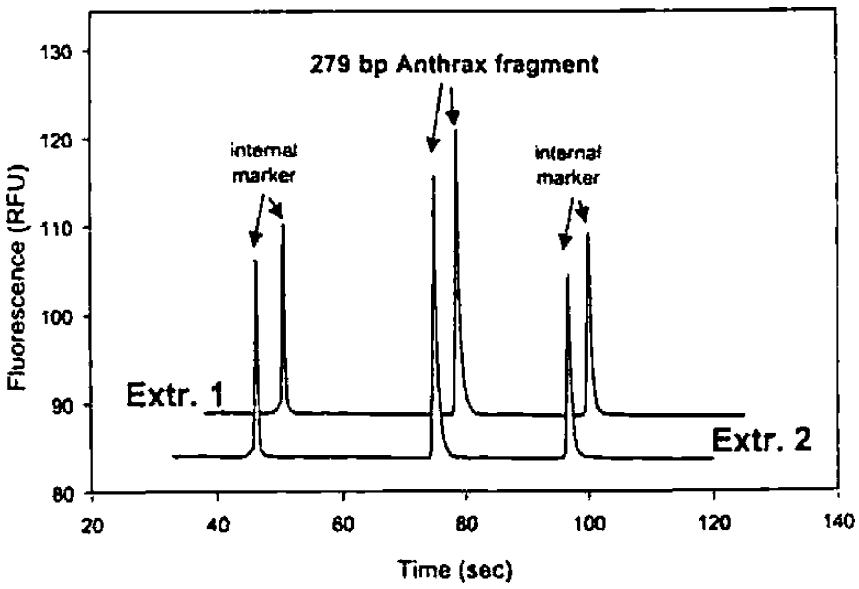

Fig. 8. Microchip-based solid-phase extraction (SPE) protocol for purifying DNA: successive extractions of bacterial DNA from the vaccine strain of *B. anthracis* (anthrax) (from Ref. [30] with permission).

Preconcentration with microfluidic devices has been performed by sample stacking or solid-phase extraction. The latter refers to processes involving retention of the target analyte by a solid phase followed by its elution in a more concentrated form. This can be accomplished by packing the microchannel with C_{18}-coated particles or by coating the channel walls with a C_{18} phase. Applicability of on-chip microscale solid-phase extraction to nitroaromatic explosives has been documented [11]. On-chip sample cleanup protocols commonly involve the use of thin ($\sim$1 μm) to exclude particulates [35].

6. Conclusions and outlook

We have described a variety of microchip protocols and devices for the detection of terrorist weapons (Table 1). Because of their versatility, efficiency, speed, high degree of integration, and ability to handle nanoliter volumes, microchip platforms have proven themselves attractive vehicles for 'counter-terrorism' assays. Clearly, 'Lab-on-a-Chip' devices offer great promise for designing miniaturized field-deployable devices (that retain the high performance of large laboratory-based instruments) and are able to deliver the analytical performance that will be required for the detection of terrorist weapons. The power and utility of such microfluidic assays will be greatly enhanced by integrating additional sample processing functions (e.g. cleanup, preconcentration) into their protocol. On-going collaborative efforts by several laboratories (including ours) are aimed at developing a self-contained completely functional multi-channel 'counter-terrorism' field-portable (hand-held) microanalyzer for providing early and timely simultaneous detection of different classes of explosives and chemical warfare agents. Such development of field-deployable inexpensive 'counter-terrorism' microanalyzers, will enable transporting the forensic laboratory to the sample source. These developments could have a major impact upon the protection of first responders and emergency personnel, on decision making, diagnosis of the nature of the attack, and gathering of forensic data, or upon the prevention of terrorist activity.

Table 1
Examples of microchip devices used for detecting terrorist weapons

Analyte	Protocol	Detector	Comments	References
Nitroaromatic explosives	CE	Fluorescence	Derivatization	[7]
Nitroaromatic explosives	CE	Amperometry	ppb detection	[9–11]
TNT	CE/immunoassay	Fluorescence	ppb detection	[15]
Ionic explosives	CE	Conductivity		[12]
Ionic and organic explosives	CE	Conductivity/amperometry		[14]
AChE inhibitors	Enzyme inhibition	Fluorescence		[17]
Cyanide		Fluorescence	Derivatization	[20]
CWA degradation products		Conductivity		[19]
B. anthracis bacterial DNA	Solid-phase extraction	Fluorescence		[30]

Acknowledgements

This research was supported by grants from NIH and from MIPT and the Office for Domestic Preparedness, US Department of Homeland Security (MIPT Award 2002-J-A-139). Points of view in this document are those of the author and do not necessarily represent the official position of the US Department of Homeland Security or MIPT.

References

[1] C. Harris, Anal. Chem. 74 (2002) 126A.
[2] D.R. Reyes, D. Iossifidis, P. Auroux, A. Manz, Anal. Chem. 74 (2002) 2623.
[3] D. Figeys, D. Pinto, Anal. Chem. 72 (2002) 330A.
[4] J. Wang, M. Pumera, M. Chatrathi, A. Escarpa, M. Musameh, Anal. Chem. 74 (2002) 1187.
[5] J. Yinon, Trends Anal. Chem. 21 (2002) 292.
[6] D. Lindner, Lab on a Chip 1 (2001) 15N.
[7] S.R. Wallenberg, C.G. Bailey, Anal. Chem. 72 (2000) 1872.
[8] J. Wang, B. Tian, E. Sahlin, Anal. Chem. 71 (1999) 5436.
[9] A. Hilmi, J.H.T. Luong, Anal. Chem. 72 (2000) 4677.
[10] J. Wang, G. Chen, M. Chatrathi, K. Shin, A. Fujishima, Anal. Chem. 75 (2003) 935.
[11] M. Smith, G.E. Collins, J. Wang, J. Chromatogr. A 991 (2003) 159.
[12] J. Wang, M. Pumera, G. Collins, Analyst 127 (2002) 719.
[13] J. Wang, G. Chen, A. Muck, Electrophoresis, in press.
[14] J. Wang, M. Pumera, Anal. Chem. 74 (2002) 5919.
[15] A. Bromberg, R.A. Mathies, Anal. Chem. 75 (2003) 1188.
[16] M. Jacoby, Chem. Eng. News 31 (March) (2003) 35.
[17] A.G. Hadd, S.C. Jacobson, J.M. Ramsey, Anal. Chem. 71 (1999) 5206.
[18] J. Wang, M.P. Chatrathi, A. Mulchandani, W. Chen, Anal. Chem. 73 (2001) 1804.
[19] J. Wang, M. Pumera, G. Collins, A. Mulchandani, Anal. Chem. 74 (2002) 6121.
[20] L. Qiu, G. Collins, Electrophoresis, submitted for publication.
[21] M. McBride, S. Gammon, M. Pitesky, T. O'Brien, T. Smith, J. Aldrich, R. Langois, B. Colston, K. Venkateswaran, Anal. Chem. 75 (2003) 1924.
[22] S. Cheng, C. Skinner, J. Taylor, S. Attiya, W. Lee, G. Picelli, D.J. Harrison, Anal. Chem. 73 (2001) 1472.
[23] W. Lee, B. Jemere, S. Attiya, N. Chiem, M. Paulson, J. Ahrend, G. Burchett, D. Bader, Y. Ning, D.J. Harrison, J. Cap. Elec. Microchip Tech. 1/2 (1999) 51.
[24] J. Wang, A. Ibanez, M. Chatrathi, A. Escarpa, Anal. Chem. 73 (2001) 5323.
[25] N. Matsuno, J. Thomas, H.B. Halsall, W.R. Heineman, Trends Anal. Chem. 21 (2002) 213.
[26] K. Sato, M. Tokeshi, H. Kimura, T. Kitamori, Anal. Chem. 73 (2001) 1213.
[27] A. Wolley, D. Hadley, P. Landre, A. deMellow, R.A. Mathies, M.A. Northrup, Anal. Chem. 68 (1996) 4081.
[28] T. Tang, M. Badal, G. Ocvirk, W. Lee, D. Bader, F. Bekkaoui, D.J. Harrison, Anal. Chem. 74 (2002) 725.
[29] Y. Liu, C. Rauch, R. Stevens, R. Lenigk, J. Yang, D. Rhine, P. Grodzinski, Anal. Chem. 74 (2000) 3063.
[30] M. Breadmore, W. Wolfe, I. Arbibal, W. Leung, D. Dickson, B. Giordano, M. Power, J. Ferrance, S. Feldman, P. Norris, J. Landers, Anal. Chem. 75 (2003) 1880.
[31] P. Belgrader, D. Hansford, G. Kovacs, K. Venkateswaran, R. Mariella, F. Milanovich, S. Nasarabadi, M. Okuzumi, F. Pourahamadi, M.A. Northrup, Anal. Chem. 71 (1999) 4232.
[32] S. Attiya, A. Jemere, T. Tang, G. Fitzpatrick, K. Seiler, N. Chiem, D.J. Harrison, Electrophoresis 22 (2001) 318.
[33] Q. Fang, G. Xu, Z. Fang, Anal. Chem. 74 (2002) 1223.
[34] J. Lichtenberg, N. de Rooij, E. Verpoorte, Talanta 56 (2002) 233.
[35] B. Broyles, S. Jacobson, J.M. Ramsey, Anal. Chem. 75 (2003) 2761.